CLAIMS

1. A water-soluble product or pharmaceutical formulation in solid or liquid form and their organic solvent-free true aqueous solutions mainly for parenteral use containing

a) a therapeutically active compound having low aqueous solubility ($<1.10^{-4}$ M/Lit, $<1.10^{-5}$ M/Lit, $<1.10^{-6}$ M/Lit) and a substantial binding affinity to plasma proteins (in the following "active substance") in an interlinked state with

b) a plasma protein fraction in controlled aggregation state

whereby the said active substance and the said protein fraction are bound to each other by way of non-covalent bonds and

optionally further containing

c) pharmaceutically acceptable and mainly parenterally acceptable watersoluble formulation additive(s) - such as water, stabilizer(s), protein aggregation controller(s).

2. A water-soluble product or pharmaceutical formulation in solid or liquid form and their organic solvent-free aqueous solutions according to claim 1 wherein the molar ratio of the active ingredient : protein is within the range of 1 : 0.05 to 1 : 100, preferably 1 : 0.1 to 1 : 50

3. A water-soluble product or human pharmaceutical formulation according to claim 1 or 2 containing a human plasma protein fraction in controlled aggregation state.

4. A water-soluble product or veterinary pharmaceutical formulation according to claim 1 or 2 containing an animal plasma protein fraction in controlled aggregation state.

5. A product or pharmaceutical formulation according to any of claims 1 to 4 containing as the plasma protein fraction a component of the natural plasma such as serum albumin or a recombinant of said plasma component.

6. A product or pharmaceutical formulation according to any of claims 1 to 5 containing as the plasma protein fraction

a natural immunoglubulin, glycoprotein, interferon and/or interleukin or a recombinant of said plasma component.

7. A product or pharmaceutical formulation according to any of claims 1 to 6 containing as the water-insoluble active substance a cytostatic such as a taxonoid, an antibiotic, vitamin, antiinflammatory, analgesic, antiviral, anticonvulsant, immunosupressant, antiepileptic, anxiolytic, hypnotic, antifungal agent, anticoagulant, lipid peroxidase inhibitor, coronary vasodilator, antiarrythmic agent, cardiotonic, uricosuric, antithrombotic, steroid hormone (progestogen, androgen, testogen) and/or photosensitizer.

8. A product or pharmaceutical formulation according to any of claims 1 to 6 containing at least one of the following active substances: amphotericin B, an adriamicine analogue, apazone, azathioprine, bromazepam, camptothecin, carbamazepine, clonazepam, cyclosporine A, diazepam, dicumarol, digitoxine, dipyridamole, disopyramide, flunitrazepam, gemfibrozil, ketochlorin, ketoconazole, miconazole, niflumic acid, oxazepam, phenobarbital, phenytoin, progesterone, propofol, ritonavir, sulfinpyrazone, suprofene, tacrolimus, tamoxifen, taxonoid, testosterone, tirilazad, trioxsalen, valproic acid, warfarin.

9. A product or pharmaceutical formulation according to any of claims 1 to 7 containing a taxonoid of the general formula I - in the formula

R^1 represents tert. butyl-oxy-carboxylic acid amide or benzoyl amide,

R^2 represents hydrogen or an acyl group preferably acetyl.

10. A product or pharmaceutical formulation according to any of claims 1 to 7 containing paclitaxel and human serum albumin, immunoglobulin, glycoprotein, interferon and/or interleukin or some other natural or recombinant human plasma protein fraction in the molar ratio of 1 : 0.05 to 1 : 100, preferably in the molar ratio of 1 : 0.1 to 1 : 50.

11. A product or pharmaceutical formulation according to any of claims 1 to 9 containing azathioprine and human serum

albumin, immunoglobulin, glycoprotein, interferon and/or interleukin or some other natural or recombinant human plasma protein fraction in the molar ratio of 1 : 0.05 to 1 : 100, preferably 1 : 0.1 to 1 : 50.

12. A formulation according to any of claims 1 to 8 containing camptothecin and human serum albumin, immunoglobulin, glycoprotein, interferon and/or interleukin or some other natural or recombinant human plasma protein fraction in the molar ratio of 1 : 0.05 to 1 : 100, preferably 1 : 0.1 to 1 : 50.

13. A formulation according to any of claims 1 to 8 containing gemfibrozil and human serum albumin, immunoglobulin, glycoprotein, interferon and/or interleukin or some other natural or recombinant human plasma protein fraction in the molar ratio of 1 : 0.05 to 1 : 100, preferably 1 : 0.1 to 1 : 50.

14. A product or pharmaceutical formulation according to any of claims 1 to 8 containing miconazole and human serum albumin, immunoglobulin, glycoprotein, interferon and/or interleukin or some other natural or recombinant human plasma protein fraction in the molar ratio of 1 : 0.05 to 1 : 100, preferably 1 : 0.1 to 1 : 50.

15. A product or pharmaceutical formulation according to any of claims 1 to 8 containing propofol and human serum albumin, immunoglobulin, glycoprotein, interferon and/or interleukin or some other natural or recombinant human plasma protein fraction in the molar ratio of 1 : 0.05 to 1 : 100, preferably 1 : 0.1 to 1 : 50.

16. A product or pharmaceutical formulation according to any of claims 1 to 8 containing tamoxifen and human serum albumin, immunoglobulin, glycoprotein, interferon and/or interleukin or some other natural or recombinant human plasma protein fraction in the molar ratio of 1 : 0.05 to 1 : 100, preferably 1 : 0.1 to 1 : 50.

17. A product or pharmaceutical formulation according to any of claims 1 to 8 containing ritonavir and human serum

albumin, immunoglobulin, glycoprotein, interferon and/or interleukin or some other natural or recombinant human plasma protein fraction the molar ratio of 1 : 0.05 to 1 : 100, preferably 1 : 0.1 to 1 : 50.

18. A pharmaceutical formulation according to any of claims 1 to 8 containing tacrolimus and human serum albumin, immunoglobulin, glycoprotein, interferon and/or interleukin or some other natural or recombinant human plasma protein fraction in the molar ratio of 1 : 0.05 to 1 : 100, preferably 1 : 0.1 to 1 : 50.

19. A pharmaceutical formulation according to any of claims 1 to 8 containing tirilazad and human serum albumin, immunoglobulin, glycoprotein, interferon and/or interleukin or some other natural or recombinant human plasma protein fraction in the molar ratio of 1 : 0.05 to 1 : 100, preferably 1 : 0.1 to 1 : 50.

20. A pharmaceutical formulation according to any of claims 1 to 8 containing trioxsalen and human serum albumin, immunoglobulin, glycoprotein, interferon and/or interleukin or some other natural or recombinant human plasma protein fraction in the molar ratio of 1 : 0.05 to 1 : 100, preferably 1 : 0.1 to 1 : 50.

21. A pharmaceutical formulation according to any of claims 1 to 20 having a solid state or having the form of an aqueous solution.

22. A pharmaceutical formulation according to any of claims 1 to 20 containing as additive an agent stabilizing the solution and/or the protein.

23. A pharmaceutical formulation according to claim 22 containing as solution- and/or protein-stabilizing agent any of the following: sodium chloride, a buffer, an alcohol such as glycerol and/or a water-soluble sugar derivative preferably mannitol, sorbitol, dulcitol.

24. Process for the preparation of a water-soluble product or pharmaceutical formulation in solid or liquid form

according to any of claims 1 to 23 or a new product according to claims 30 to 37 and their organic solvent-free true aqueous solutions characterized by
preparing a true aqueous solutions by way of

a) dissolving the therapeutically active compound having low aqueous solubility (<1.10^{-4} M/Lit, <1.10^{-5} M/Lit, <1.10^{-6} M/Lit) and a substantial binding affinity to plasma proteins ("active substance") in a water-miscible, pharmaceutically acceptable organic solvent,

b) combining said solution with the aqueous solution of the plasma protein fraction in controlled aggregation state

c) and optionally with a further pharmaceutically acceptable water-soluble auxiliary additive - such as a protein aggregation controller and/or a stabilizer -

whereby a true solution is obtained containing the said active substance and the said protein fraction bound together by way of non-covalent bonds;

d) removing the organic solvent and optionally the water preferably by ultrafiltering, dialysing, diafiltrating and/or lyophilising the solution or its concentrate or by combination of these treatments
whereby a homogeneous, water-soluble liquid or solid pharmaceutical product is obtained containing the active substance interlinked with the plasma protein fraction;

e) optionally dissolving the solid product in water or diluting the liquid product with water whereby a clear, true aqueous solution, free of any organic solvent is obtained which is suitable for therapeutical administration and

f) optionally finishing this product into a parenteral formulation (dosage form) for direct use.

25. Process for the preparation of a water-soluble product or pharmaceutical formulation in solid or liquid form according to any of claims 1 to 23 or a new product according to claims 30 to 37 and their organic solvent-free true aqueous solutions characterized by

a) dissolving the therapeutically active compound in a water-miscible, pharmaceutically acceptable organic solvent,

b) combining said solution with the aqueous solution of the selected plasma protein fraction in controlled aggregation state,

c) said solution containing optionally a further pharmaceutically acceptable auxiliary additive - such as a protein aggregation controller and/or a stabilizer -

whereby a true solution is obtained containing the said active substance and the said protein fraction bound together by way of non-covalent bonds;

d) removing the organic solvent and lyophilising the solution or its concentrate.

26. A process according to step a) of any of claims 23 to 25 characterized by using to dissolve the active substance a solvent having the following properties:

a) it is capable to completely dissolve the active substance in its mixture with water and

b) its mixture with <50% of water does not denaturalize the protein employed.

27. A process according to claim 26 characterized by using as the solvent any of the group consisting of an aliphatic $C_{(2-4)}$ monoalcohol or polyalcohol, 70 - 100% ethanol, dimethyl formamide, methyl formamide.

28. A process according to step a) of claim 23 to 27 characterized by using as protein aggregation controller or stabilizer and/or solution stabilizing auxiliary additive any of the following agents: water, sodium chloride, a buffer, a poly- alcohol such as glycerol and/or a water-soluble sugar derivative preferably mannitol, sorbitol and/or dulcitol.

29. A process according to step a) of any of claims 23 to 28 characterized by using paclitaxel and a component of the natural plasma such as serum albumin, an immunoglubulin, glycoprotein, interferon and/or interleukin or a recombinant of the same.

30. A homogeneous, solid, water-soluble product consisting of at least one active substance having low aqueous

solubility (<1.10^{-4} M/Lit, <1.10^{-5} M/Lit, <1.10^{-6} M/Lit) of the group amphotericin B, an adriamicine analogue, apazone, azathioprine, bromazepam, camptothecin, carbamazepine, clonazepam, cyclosporine A, diazepam, dicumarol, digitoxine, dipyridamole, disopyramide, flunitrazepam, gemfibrozil, ketochlorin, ketoconazole, miconazole, niflumic acid, oxazepam, phenobarbital, phenytoin, progesterone, propofol, ritonavir, sulfinpyrazone, suprofene, tacrolimus, tamoxifen, taxonoid, testosterone, tirilazad, trioxsalen, valproic acid and/or warfarin
and also consisting of at least one protein of the group human serum albumin, immunoglobulin, glycoprotein, interferon and/or interleukin or some other natural or recombinant human plasma protein fraction
where the said active substance and the said protein fraction are bound to each other by way of non-covalent bonds and wherein the molar ratio of the said active substance and the said protein fraction is within the range of 1 : 0.05 to 1 : 100, preferably of 1 : 0.1 to 1 : 50.

31. A homogeneous, solid, water-soluble product according to claim 30 consisting of a taxonoide of the general formula I - in the formula

R^1 represents tert. butyl-oxy-carboxylic acid amide or benzoyl amide,

R^2 represents hydrogen or any acyl group preferably acetyl -

and of a plasma protein fraction.

32. A homogeneous, solid, water-soluble product according to claim 30 consisting of paclitaxel and human serum albumin, recombinant human plasma albumin and/or γ-globulin.

33. A homogeneous, solid, water-soluble product according to claim 30 consisting of amphotericin B and human serum albumin, recombinant human plasma albumin and/or γ-globulin.

34. A homogeneous, solid, water-soluble product according to claim 30 consisting of camptothecin and human serum albumin, recombinant human plasma albumin and/or γ-

globulin.

35. A homogeneous, solid, water-soluble product according to claim 28 consisting of carbamazepin and human serum albumin, recombinant human plasma albumin and/or γ-globulin.

36. A homogeneous, solid, water-soluble product according to claim 28 consisting of cyclosporin A and human serum albumin, recombinant human plasma albumin and/or γ-globulin.

37. A homogeneous, solid, water-soluble product according to claim 30 consisting of propofol and human serum albumin, recombinant human plasma albumin and/or γ-globulin.

38. Method of treatment of human or veterinary patients with a therapeutically active substance having low aqueous solubility ($<1.10^{-4}$ M/Lit, $<1.10^{-5}$ M/Lit, $<1.10^{-6}$ M/Lit) and having substantial plasma protein affinity characterized by administering to a patient in need of a treatment with said active substance an effective dose of the product or pharmaceutical formulation according to or prepared according to any of claims 1 to 37.

39. Method of treatment of human or veterinary patients with a therapeutically active substance having low aqueous solubility ($<1.10^{-4}$ M/Lit, $<1.10^{-5}$ M/Lit, $<1.10^{-6}$ M/Lit) and having substantial plasma protein affinity characterized by parenterally administering to a patient in need of a treatment with said active substance an effective dose of the following products preferably using the following dose ranges respectively (calculated on the active substance): paclitaxel/albumin 70 - 280 mg/treatment; propofol/albumin 6 - 10 mg/kg/hour; camptothecin/albumin, gemfibrozil/albumin, cyclosporin A/ albumin 3 - 5 mg/kg/day; amphothericin B/ albumin up to 1.5 mg/kg/day, whereby the same dose ranges are used for compounds containig the recombinant proteins respectively.

40. Method for parenteral delivery in therapeutic use of pharmaceutically active ingredients with poor solubility

($<1.10^{-4}$ M/Lit, $<1.10^{-5}$ M/Lit, $<1.10^{-6}$ M/Lit) and substantial affinity for binding to plasma proteins characterized by administering to a patient in need of a treatment with said active substance an effective dose of the composition according to or prepared according to any of claims 1 to 29.

41. A product or method substantially as described in any of the examples.